Complete Summary

GUIDELINE TITLE

Lymphoma - non-Hodgkin´s.

BIBLIOGRAPHIC SOURCE(S)

Lymphoma - non-Hodgkin's. Philadelphia (PA): Intracorp; 2005. various p. [18 references]

GUIDELINE STATUS

This is the current release of the guideline.

All Intracorp guidelines are reviewed annually and updated as necessary, but no less frequently than every 2 years. This guideline is effective from April 1, 2005 to April 1, 2007.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Non-Hodgkin's lymphoma

- B-cell lymphoma
- Precursor B/T-cell lymphoma
- T-cell lymphoma

GUIDELINE CATEGORY

Diagnosis
Evaluation

Management
Treatment

CLINICAL SPECIALTY

Family Practice
Hematology
Internal Medicine
Oncology
Radiation Oncology

INTENDED USERS

Allied Health Personnel
Health Care Providers
Health Plans
Hospitals
Managed Care Organizations
Utilization Management

GUIDELINE OBJECTIVE(S)

To present recommendations for the diagnosis, treatment, and management of non-Hodgkin's lymphoma that will assist medical management leaders to make appropriate benefit coverage determinations

TARGET POPULATION

Individuals with non-Hodgkin's lymphoma

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Physical examination and assessment of signs and symptoms
2. Diagnostic tests:
    - Lymph node biopsy with removal of entire suspicious node
    - Histopathology and immunophenotyping
    - Bilateral bone marrow biopsies
    - Lymphangiogram
    - Computerized tomography (CT) scans of abdomen, bone, chest, head, liver, and spleen
    - Chest x-ray (CXR)
    - Magnetic resonance imaging (MRI), if indicated
    - Lumbar puncture
    - Laparotomy
    - Blood work (alkaline phosphatase [ALP] and glutamyl transferase [GGT])

Management/Treatment

1. "Watchful waiting"
2. Chemotherapy: cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), alkylating chemotherapy
3. Allogeneic and autologous bone marrow transplantation
4. Radiation therapy
5. Growth factor, monoclonal antibodies (under investigation)
6. Physical therapy, if indicated
7. Referral to specialists
8. Case management strategies, including case initiation, case management focus, and discharge

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches were performed of the following resources: reviews by independent medical technology assessment vendors (such as the Cochrane Library, HAYES); PubMed; MD Consult; the Centers for Disease Control and Prevention (CDC); the U.S. Food and Drug Administration (FDA); professional society position statements and recommended guidelines; peer reviewed medical and technology publications and journals; medical journals by specialty; National Library of Medicine; Agency for Healthcare Research and Quality; Centers for Medicare and Medicaid Services; and Federal and State Jurisdictional mandates.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

A draft Clinical Resource Tool (CRT or guideline) is prepared by a primary researcher and presented to the Medical Technology Assessment Committee or the Intracorp Guideline Quality Committee, dependent upon guideline product type.

The Medical Technology Assessment Committee is the governing body for the assessment of emerging and evolving technology. This Committee is comprised of a Medical Technology Assessment Medical Director, the Benefit and Coverage Medical Director, CIGNA Pharmacy, physicians from across the enterprise, the Clinical Resource Unit staff, Legal Department, Operations, and Quality. The Intracorp Guideline Quality Committee is similarly staffed by Senior and Associate Disability Medical Directors.

Revisions are suggested and considered. A vote is taken for acceptance or denial of the CRT.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Comparison with Guidelines from Other Groups
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Diagnostic Confirmation

Subjective Findings

Symptoms and clinical findings vary based upon local effects of tumor growth.

- Painless peripheral swellings
- Signs of mediastinal disease:
    - Persistent cough
    - Chest discomfort
- Signs of abdominal disease
    - Abdominal mass
    - Bowel obstruction
    - Sensation of gastric fullness
    - Persistent discomfort
- "B symptoms," such as:
    - Night sweats
    - Unintentional weight loss
    - Fever of unknown origin (much less common in non-Hodgkin's lymphoma [NHL] than in Hodgkin's lymphoma)
- Weakness or numbness in extremities

Objective Findings

- Anemia
- Enlarged lymph nodes, isolated or widespread
- Intermittent fever, that comes and goes in periods of days or weeks
- Peripheral lymphadenopathy
- Hepatomegaly, splenomegaly, or palpable abdominal masses
- Superior vena cava (SVC) syndrome
- Unintentional weight loss
- Central nervous system (CNS) symptoms, such as focal weakness or paresthesias, often the primary presentation in patients with human immunodeficiency virus (HIV)

Diagnostic Tests

- Lymph node biopsy (see gold standard for identification of NHL)
    - During biopsy, removal of entire suspicious node(s) is essential and preferred to relying on simple needle biopsy or incisional biopsy.
    - Histopathology and immunophenotyping aid in determining grade of malignancy, treatment response, and prognosis:
        - Lymphocytes predominate, minimal nodal involvement equals favorable prognosis, low grade tumor
        - "Mixed cellularity," nodular sclerosis present: intermediate prognosis equals intermediate grade tumor
        - Low lymphocyte count, tumor cells throughout lymph nodes equals poor prognosis, high grade tumor
- Bilateral bone marrow biopsies
    - After confirmed diagnosis, bone marrow biopsy may be done to stage NHL and to identify occult cancer sites.
        - Iliac crests are used as marrow sources.
    - Flow cytometry is recommended.
- Lymphangiogram

- Computerized tomography (CT) scans of abdomen, bone, chest, head, liver, spleen (see the Intracorp Imaging guidelines)
    - After confirmed diagnosis, head, chest, or abdomen scans may be done to identify distant disease.
    - To further evaluate NHL, bone scans of long bones, vertebrae, and pelvis may be indicated.
    - Accurate identification of organ/systemic involvement is extremely important for treatment decisions.
- Chest x-ray (CXR)
    - Often performed to rule-out/rule-in enlarged lymph nodes in thorax
- Magnetic resonance imaging (MRI)
    - MRI should be undertaken only if CT is inconclusive (see the Intracorp Imaging guideline).
- Lumbar puncture (LP)
    - LP is performed on patients at high risk for CNS involvement (seen in HIV-associated NHL), when less invasive methods did not provide information sufficient to coordinate treatment.
- Laparotomy
    - Although not generally performed in uncomplicated situations, laparotomy may offer valuable information about the extent of disease in severe cases when less invasive methods were inconclusive.
    - Also therapeutic for removal of sizable tumors that may be causing symptoms
- Additional blood work that may be performed
    - Alkaline phosphatase (ALP). Normals (adult): 17 to 142 U/L
    - Glutamyl transferase (GGT). Normals - Men: 5 to 85 U/L; Women: 5 to 55 U/L
        - Abnormal results may indicate metastatic disease.
        - Certain chemotherapy agents are contraindicated if liver chemistries are altered.
    - Molecular genetic studies an area of current investigation

Differential Diagnosis

- Infections, including staphylococcal or streptococcal lymphadenitis from local infections; toxoplasmosis; mycobacterial disease; tularemia; syphilis; mononucleosis; and HIV
- Other malignancies, such as Hodgkin's lymphoma and metastatic spread from any primary malignancy
- Sarcoidosis

<u>Treatment Options</u>

- Low-grade NHL, generally considered indolent and non-curable
    - Asymptomatic, no initial treatment may be necessary, "watchful waiting"
- Disease that has progressed:
    - Basic chemotherapy regimen: cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) is standard recommendation, unless comorbid illness(es) would make its use inappropriate.
    - CHOP plus rituximab - the first monoclonal antibody approved by the U.S. Food and Drug Administration (FDA) to treat cancers.

    - Alkylating chemotherapy (see the Intracorp guideline Chemotherapy)
    - Combination chemotherapy, such as cyclophosphamide, vincristine, and prednisone (CVP) or CHOP (CVP plus adriamycin)
    - Chemotherapy Care Setting: clinic or free-standing outpatient, physician's office, or home care; may be acute inpatient, subacute/skilled nursing facility inpatient, or hospice inpatient setting if patient acutely ill, severely deconditioned, etc.
- Allogeneic and autologous bone marrow transplantation, for relapse after standard treatment (see the Intracorp guideline Bone Marrow Transplantation)
    - Transplant Care Setting: acute inpatient for induction and consolidation; may be outpatient for pre-testing; outpatient or home care for maintenance
- Radiation therapy, for early-stage localized lymph node disease or for later-stage disease in conjunction with chemotherapy
    - Radiation Care Setting: clinic or free-standing outpatient; unless acute illness/deconditioning necessitate acute inpatient, subacute/skilled nursing facility inpatient, or hospice inpatient
    - NOTE: Recent studies show adding radiation therapy and reducing chemotherapy courses may improve outcomes and decrease toxicities in localized but histologically unfavorable NHL disease.
- HIV-related lymphomas (often the most aggressive NHL subtype)
    - Aggressive regimens, such as salvage therapy attempts, often have discouraging outcomes.
    - Use of growth factor to stimulate white and red blood cell generation in HIV -infected NHL patients
    - Treatment modalities under study include monoclonal antibodies directed at lymphoma cells and interferon with high-dose chemotherapy, but no standards have yet been established.

Duration of Medical Treatment

- Medical - Optimal: 14 day(s)
    - Maximal duration is lifetime.

Additional information regarding primary care visit schedules, referral options, specialty care, and physical therapy is provided in the original guideline document.

The original guideline document also provides a list of red flags that may affect disability duration, and return to work goals, including:

- After chemotherapy or combined therapy
- After bone marrow transplant

Note: Some patients with this condition may never return to work.

Case Management Directives (refer to the original guideline for detailed recommendations)

Case Initiation

Establish Case

- Document baseline information, history, key physical findings, patient's understanding, and safety factors.
- Refer to Chemotherapy Chart in the original guideline document.
- The American Joint Committee on Cancer encourages use of the "TNM" classification system (T=primary tumor size; N=lymph node involvement; M=metastasis).
- Provide contact information for local and national support groups.

Coordinate Care

- Advocate for patient by managing utilization and charges.
- Document treatment plan.

Case Management Focus

Activity Deficit

- Document activity alteration as none, mild, moderate, severe, dependent, or bed-bound (based on most recent performance status) and interventions required.

Chemotherapy Intolerance

- Assess status, acute versus chronic, of toxic side effects on rapidly growing tissues, including bone marrow, epithelium, hair, sperm, and document intervention recommended.

Hemodynamic Instability

- Document bleeding complications, severity, and intervention recommended.

Immune Compromised

- Document establishment of protective isolation measures for a white blood cells count (WBC) less than 1,000/mm^3, implying dangerous susceptibly to infection.

Inadequate Nutrition

- Use optimal goal of remaining within 10% of pretreatment weight to document hydration and nutrition deficit as mild, moderate, severe and response needed.

Mental and Emotional Alteration

- Ensure accurate diagnosis of any change in mental status.
- Document baseline or optimal mental and emotional functioning and their alterations due to cancer presence, comorbidity, surgery, or treatments.

- Assess and respond appropriately to the degree of debility caused by alterations listed in the original guideline document through benefit coordination or community resource activation.

Pain Control

- Document optimal pain management by characterizing severity and interventions undertaken to remedy or manage pain.

Oncologic Emergencies

- Immediately report to the physician or activate emergency medical technician (EMT) system as needed for signs and symptoms of CNS infection (common, major problem), such as confusion, fever, hyperreflexia, nausea, nuchal rigidity, and vomiting.
- Document presence of or developing oncologic emergencies and report to attending physician, surgeon, or activate EMT system as necessary.

Radiation Intolerance

- Document presence and severity of radiation side effects.
- Initiate early interventions for complications of radiation therapy.

Respiratory Instability

- Document respiratory deficit as mild, moderate, severe, and dependent, and respiratory rehabilitation enhancement measures.

Skin Integrity Deficit

- Assess barriers to rehabilitation involving alterations in skin integrity and interventions necessary to expedite recuperation.
- Document severity of skin integrity disruption.

Terminal Care

- Document optimal comfort measures and palliative care initiatives.

Discharge

Discharge from Case Management (CM)

- Document return to independence or stabilized functional status and closing conversations with patient, caregiver, physician, pharmacist, and care providers.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis, treatment, and management of non-Hodgkin's lymphoma that assist medical management leaders to make appropriate benefit coverage determinations

POTENTIAL HARMS

Refer to the Case Management Focus section of the "Major Recommendations" field for information on potential complications and strategies to address them, or refer to the original guideline document.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Lymphoma - non-Hodgkin's. Philadelphia (PA): Intracorp; 2005. various p. [18 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1997 (revised 2005)

GUIDELINE DEVELOPER(S)

Intracorp - Public For Profit Organization

SOURCE(S) OF FUNDING

Intracorp

GUIDELINE COMMITTEE

CIGNA Clinical Resources Unit (CRU)
Intracorp Disability Clinical Advisory Team (DCAT)
Medical Technology Assessment Committee (MTAC)
Intracorp Guideline Quality Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

All Intracorp guidelines are reviewed annually and updated as necessary, but no less frequently than every 2 years. This guideline is effective from April 1, 2005 to April 1, 2007.

GUIDELINE AVAILABILITY

Electronic copies: Intracorp guidelines are available for a licensing fee via a password protected, secure Web site at www.intracorp.com.

Reprints of complete guideline content may be purchased for $35.00 per title (plus tax in TX at 8.25% and CT at 1.0%). Please send e-mail request to lbowman@mail.intracorp.com.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Policies and procedures. Medical Technology Assessment Committee Review Process. Philadelphia (PA): Intracorp; 2004. 4 p.
- Online guideline user trial. Register for Claims Toolbox access at www.intracorp.com.

Licensing information and pricing: Available from Intracorp, 1601 Chestnut Street, TL-09C, Philadelphia, PA 19192; e-mail: lbowman@mail.intracorp.com.

Reprints of complete guideline content may be purchased for $35.00 per title (plus tax in TX). Please send e-mail request to mbraytenbah@mail.intracorp.com.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on May 25, 2005. The information was verified by the guideline developer on June 7, 2005.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 10/2/2006